UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Note to Reader

Background: As part of its effort to involve the public in the implementation of the Food Quality Protection Act of 1996 (FQPA), which is designed to ensure that the United States continues to have the safest and most abundant food supply. EPA is undertaking an effort to open public dockets on the organophosphate pesticides. These dockets will make available to all interested parties documents that were developed as part of the U.S. Environmental Protection Agency's process for making reregistration eligibility decisions and tolerance reassessments consistent with FQPA. The dockets include preliminary health assessments and, where available, ecological risk assessments conducted by EPA, rebuttals or corrections to the risk assessments submitted by chemical registrants, and the Agency's response to the registrants' submissions.

The analyses contained in this docket are preliminary in nature and represent the information available to EPA at the time they were prepared. Additional information may have been submitted to EPA which has not yet been incorporated into these analyses, and registrants or others may be developing relevant information. It's common and appropriate that new information and analyses will be used to revise and refine the evaluations contained in these dockets to make them more comprehensive and realistic. The Agency cautions against premature conclusions based on these preliminary assessments and against any use of information contained in these documents out of their full context. Throughout this process, If unacceptable risks are identified, EPA will act to reduce or eliminate the risks.

There is a 60 day comment period in which the public and all interested parties are invited to submit comments on the information in this docket. Comments should directly relate to this organophosphate and to the information and issues available in the information docket. Once the comment period closes, EPA will review all comments and revise the risk assessments, as necessary.

These preliminary risk assessments represent an early stage in the process by which EPA is evaluating the regulatory requirements applicable to existing pesticides. Through this opportunity for notice and comment, the Agency hopes to advance the openness and scientific soundness underpinning its decisions. This process is designed to assure that America continues to enjoy the safest and most abundant food supply. Through implementation of EPA's tolerance reassessment program under the Food Quality Protection Act, the food supply will become even safer. Leading health experts recommend that all people eat a wide variety of foods, including at least five servings of fruits and vegetables a day.

Note: This sheet is provided to help the reader understand how refined and developed the pesticide file is as of the date prepared, what if any changes have occurred recently, and what new information, if any, is expected to be included in the analysis before decisions are made. **It is not meant to be a summary of all current information regarding the chemical.** Rather, the sheet provides some context to better understand the substantive material in the docket (RED chapters, registrant rebuttals, Agency responses to rebuttals, etc.) for this pesticide.

Further, in some cases, differences may be noted between the RED chapters and the Agency's comprehensive reports on the hazard identification information and safety factors for all organophosphates. In these cases, information in the comprehensive reports is the most current and will, barring the submission of more data that the Agency finds useful, be used in the risk assessments.

Jack E. Housenger, Acting Director
Special Review and Reregistration Division

MEMORANDUM

Subject: Acute and Chronic Dietary Exposure and Risk Analysis for Phostebupirim (PC code 129086); DP Barcode D254707

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Action Requested

An acute and chronic dietary exposure and risk assessment was requested to determine the risks associated with the reregistration uses of Phostebupirim on corn. In this assessment, there are no changes to published tolerances.

Executive Summary

In this analysis, a Tier I acute and chronic dietary exposure and risk assessment was performed to determine the risk associated with the uses of phostebupirim on sweet corn and field corn which are supported through the re-registration process. The assessment utilized tolerance level residues to estimate the dietary exposure of phostebupirim in the diets of the U.S. population as well as certain sub-populations and assumed that 100% of the crop(s) were treated with the chemical. The risks associated with these uses do not exceed the Agency's level of concern. The acute dietary risk is 5% of the RfD (PAD) for the most highly exposed sub-population, children 1-6. The chronic dietary risk is 17% of the RfD (PAD) for the most highly exposed sub-population, children 1-6.

Toxicological Endpoints

The Hazard Identification Assessment and Review Committee (HIARC) discussed the hazard endpoint selection for phostebupirim acute and chronic dietary exposure and risk assessment (R. Fricke, 3/17/99). Prior to this meeting, Bayer Corporation submitted acute and subchronic neurotoxicity studies in the rat which were reviewed and found to be acceptable. The registrant satisfied all requirements for acute and subchronic neurotoxicity studies in the rat. Therefore, the HIARC recommended to the FQPA Safety Factor Committee that the FQPA factor not be retained (FQPA factor = 1). In a meeting on March 29, 1999 the FQPA committee accepted the HIARC recommendation and removed the safety factor. The following are the toxicological endpoints used for the acute and chronic dietary risk assessment.

	Acute	Chronic
Critical Study	Acute Neurotoxicity Study in the Rat	1-year Dog Feeding Study
Endpoint	Plasma and RBC ChEI[a] at 1.5 hr post-dosing	Plasma, RBC and brain ChEI[a]
NOAEL	0.5 mg/kg (LOAEL) NOAEL not achieved in males	0.02 mg/kg/day
Uncertainty Factor	UF=300 100x inter- and intraspecies variation and 3x lack of NOAEL	UF=100 100X inter- and intraspecies variation
RfD	0.002 mg/kg	0.0002 mg/kg/day
FQPA Safety Factor	1 (FQPA Safety Factor removed)	1 (FQPA Safety Factor removed)
PAD[b]	0.002 mg/kg (Same as acute RfD)	0.0002 mg/kg/day (Same as chronic RfD)

a ChEI - cholinesterase inhibition
b PAD = population adjusted dose RfD/FQPA Safety Factor

Residue Information

The published tolerances for phostebupirim are located at 40 CFR 180.483. Tolerances are listed for:

Corn, forage and fodder0.01 ppm
Corn, pop0.01 ppm
Corn, sweet0.01 ppm

There are no additions or revocations of crops or crop groups included in the re-registration document nor are there any recommended changes to the tolerance. The last risk assessment performed for phostebupirim (HED Risk Assessment, 2/16/95) stated that metabolism studies demonstrate that there is no reasonable likelihood of secondary residues occurring in meat, milk,

poultry, or eggs as a result of the use of phostebupirim of corn (category 3 of 40 CFR 180.6(a) applies). Therefore, this dietary assessment includes only tolerance level residues on the above corn products.

The acute and chronic dietary exposure assessment used published tolerance level residue values and assumed 100% of the crop is treated. In this case, the acute and the chronic residue values are identical.

Results and Discussion

The acute and chronic dietary exposure and risk assessments were performed using the Dietary Exposure Evaluation Model (DEEM ™). DEEM can be used to estimate exposure to constituents in foods comprising the diets of the US population, including population subgroups. The software contains food consumption data from the USDA Continuing Survey of Food Intake by Individuals (CFSII) from 1989-1992. A summary of the residue information considered in this acute and chronic analysis is attachment 1.

Acute Exposure Analysis (Tier I)
The detailed acute dietary risk analysis estimates the distribution of single day exposures for the overall U.S. population and certain subgroups. The analysis evaluates exposure to the chemical for each food commodity and assumes uniform distribution of phostebupirim in the food supply.

The aRfD is derived from the lowest exposure at which there are statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group along with the application of uncertainty factors. The percent of the aRfD is calculated as the ratio of the exposure value to the RfD (exposure/aRfD x 100 = % aRfD). The population adjusted dose (PAD) is the ratio of the aRfD and the FQPA safety factor for sensitivity of infants and children, for all populations which include infants and children. For phostebupirim, since the HED FQPA Safety Factor Committee determined to remove the 10x Safety Factor, the RfD is identical to the PAD. For the acute dietary exposure analysis of phostebupirim, exposure (consumption) was compared to an acute population adjusted dose of 0.002 mg/kg-bw/day (B. Tarplee, 3/30/99) which reflects an FQPA factor of 1. The acute dietary risks associated with the use of phostebupirim on corn do not exceed the Agency's level of concern. The results of this analysis is shown in attachment 2.

Chronic Exposure Analysis (Tier I)

A chronic exposure analysis was performed utilizing the DEEM ™ exposure modeling software. The input values include the reassessed tolerance level residues for commodities on which phostebupirim is used.

The RfD is derived from an exposure level at which there are no statistically or biologically significant increases in the frequency or severity of adverse effects between the exposed

population and its appropriate control along with the application of uncertainty factors. The percent of the RfD is calculated as the ratio of the exposure value to the RfD (exposure/RfD x 100 = % RfD). The population adjusted dose (PAD) is the ratio of the RfD and the FQPA safety factor for sensitivity of infants and children, for all populations which include infants and children. For phostebupirim, since the HED FQPA Safety Factor Committee determined to remove the 10x Safety Factor, the RfD is identical to the PAD. Exposure (consumption) was compared to the chronic population adjusted dose of 0.0002 mg/kg-bw/day (B. Tarplee, 3/30/99) which reflects an FQPA safety factor of 1. The chronic dietary risk associated with the use of phostebupirim on corn do not exceed the Agency's level of concern. The results of this analysis are shown in attachment 3.

Attachment 1 - Residue File Listing
Attachment 2 - Acute Dietary Exposure and Risk Assessment
Attachment 3 - Chronic Dietary Exposure and Risk Assessment

ATTACHMENT 1

U.S. Environmental Protection Agency Ver. 6.12
DEEM89N CHRONIC analysis for PHOSTEBUPIRIM (1989-92 data)
Residue file name: 129086R Adjustment factor #2 NOT used.
Analysis Date 03-25-1999 Residue file dated: 03-25-1999/15:21:21/8
Reference dose (RfD, CHRONIC) = 0.000200 mg/kg body-wt/day
COMMENT 1: published tol.; no changes in reassessment

Residue file listing

Food Code	EPA Code	Crop Group	Food Name	Residue (ppm)	Adj. Fctrs #1	#2
237	15004AA	O	CORN/POP	0.010000	1.00	1.00
238	15005AA	O	CORN/SWEET	0.010000	1.00	1.00
266	24002EA	O	CORN GRAIN-ENDOSPERM	0.010000	1.00	1.00
267	24002HA	O	CORN GRAIN-BRAN	0.010000	1.00	1.00
268	24002SA	O	CORN GRAIN/SUGAR/HFCS	0.010000	1.50	1.00
289	27002OA	O	CORN GRAIN-OIL	0.010000	1.00	1.00
388	24002MO	O	CORN GRAIN/SUGAR-MOLASSES	0.010000	1.50	1.00

ATTACHMENT 2

U.S. Environmental Protection Agency Ver. 6.27
DEEM ACUTE analysis for PHOSTEBUPIRIM (1989-92 data)
Residue file name: 129086r.R91 Adjustment factor #2 NOT used.
Analysis Date: 03-25-1999/15:33:52 Residue file dated: 03-25-1999/15:21:21/8
Acute Reference Dose (aRfD) = 0.002000 mg/kg body-wt/day
Run Comment: published tol.; no changes in reassessment

Summary calculations:

	95th Percentile Exposure	% aRfD	99th Percentile Exposure	% aRfD	99.9 Percentile Exposure	% aRfD
U.S. pop - all seasons:	0.000047	2.33	0.000085	4.25	0.000149	7.45
U.S. pop - spring season:	0.000044	2.19	0.000083	4.14	0.000139	6.95
U.S. pop - summer season:	0.000049	2.45	0.000092	4.60	0.000158	7.89
U.S. pop - autumn season:	0.000046	2.29	0.000085	4.23	0.000149	7.44
U.S. pop - winter season:	0.000048	2.38	0.000082	4.10	0.000143	7.15
Northeast region:	0.000043	2.14	0.000082	4.09	0.000135	6.76
Midwest region:	0.000051	2.55	0.000091	4.53	0.000153	7.65
Southern region:	0.000047	2.37	0.000085	4.25	0.000152	7.62
Western region:	0.000045	2.23	0.000079	3.94	0.000148	7.41
Hispanics:	0.000045	2.27	0.000088	4.38	0.000138	6.89
Non-hispanic whites:	0.000046	2.28	0.000082	4.11	0.000148	7.42
Non-hispanic blacks:	0.000054	2.68	0.000093	4.65	0.000149	7.47
Non-hispanic other:	0.000044	2.21	0.000078	3.88	0.000138	6.92
All infants (<1 year):	0.000081	4.03	0.000122	6.08	0.000206	10.32
Nursing infants (<1 year):	0.000025	1.26	0.000037	1.87	0.000041	2.07
Non-nursing infants (<1 yr):	0.000089	4.46	0.000137	6.85	0.000213	10.63
Children (1-6 years):	0.000096	4.79	0.000142	7.09	0.000214	10.68
Children (7-12 years):	0.000068	3.39	0.000093	4.65	0.000139	6.97
Females (13+/preg/not nsg):	0.000027	1.35	0.000035	1.75	0.000051	2.55

ATTACHMENT 2 (cont.)

U.S. Environmental Protection Agency Ver. 6.27
DEEM ACUTE analysis for PHOSTEBUPIRIM (1989-92 data)
Residue file name: 129086r.R91 Adjustment factor #2 NOT used.
Analysis Date: 03-25-1999/15:33:52 Residue file dated: 03-25-1999/15:21:21/8
Acute Reference Dose (aRfD) = 0.002000 mg/kg body-wt/day

Summary calculations:

	95th Percentile Exposure	% aRfD	99th Percentile Exposure	% aRfD	99.9 Percentile Exposure	% aRfD
Females (13+/nursing):	0.000037	1.84	0.000045	2.25	0.000047	2.37
Females (13-19 yrs/np/nn):	0.000038	1.91	0.000064	3.19	0.000096	4.80
Females (20+ years/np/nn):	0.000027	1.37	0.000047	2.35	0.000087	4.34
Females (13-50 years):	0.000031	1.56	0.000050	2.48	0.000090	4.49
Males (13-19 years):	0.000048	2.40	0.000080	3.99	0.000110	5.51
Males (20+ years):	0.000030	1.51	0.000048	2.39	0.000077	3.87
Seniors (55+):	0.000025	1.23	0.000039	1.95	0.000085	4.26
Pacific Region:	0.000041	2.07	0.000071	3.56	0.000130	6.51

ATTACHMENT 3

U.S. Environmental Protection Agency Ver. 6.12
DEEM89N CHRONIC analysis for PHOSTEBUPIRIM (1989-92 data)
Residue file name: 129086R Adjustment factor #2 NOT used.
Analysis Date 03-25-1999 Residue file dated: 03-25-1999/15:21:21/8
Reference dose (RfD, CHRONIC) = 0.000200 mg/kg body-wt/day
COMMENT 1: published tol.; no changes in reassessment

Total exposure by population subgroup

Population Subgroup	Total Exposure mg/kg body wt/day	Total Exposure Percent of Rfd
U.S. Pop - 48 states - all seasons	0.000015	7.4%
U.S. Population - spring season	0.000014	7.2%
U.S. Population - summer season	0.000016	7.8%
U.S. Population - autumn season	0.000015	7.5%
U.S. Population - winter season	0.000014	7.0%
Northeast region	0.000014	6.8%
Midwest region	0.000016	7.8%
Southern region	0.000016	7.8%
Western region	0.000014	6.8%
Pacific Region	0.000013	6.4%
Hispanics	0.000015	7.3%
Non-hispanic whites	0.000015	7.3%
Non-hispanic blacks	0.000017	8.4%
Non-hispanic other than black or white	0.000013	6.6%
All infants (<1 year)	0.000018	8.9%
Nursing infants (<1 year)	0.000006	2.9%
Non-nursing infants (<1 year)	0.000023	11.5%
Children (1-6 years)	0.000035	17.6%
Children (7-12 years)	0.000027	13.3%
Females (13-19 yrs/not preg. or nursing)	0.000015	7.3%
Females (20+ years/not preg. or nursing)	0.000010	4.8%
Females (13-50 years)	0.000011	5.5%
Females (13+/pregnant/not nursing)	0.000011	5.3%
Females (13+/nursing)	0.000012	6.0%
Males (13-19 years)	0.000019	9.3%
Males (20+ years)	0.000011	5.4%
Seniors (55+)	0.000009	4.3%